

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 7/16, 7/18</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 98/22079</b> <b>(43) International Publication Date:</b> 28 May 1998 (28.05.98)
<b>(21) International Application Number:</b> PCT/US97/21029 <b>(22) International Filing Date:</b> 18 November 1997 (18.11.97)  <b>(30) Priority Data:</b> 08/754,577 21 November 1996 (21.11.96) US  <b>(71) Applicant:</b> THE PROCTER & GAMBLE COMPANY [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US).  <b>(72) Inventors:</b> WHITE, Donald, James, Jr.; 5690 Bordeaux Way, Fairfield, OH 45014 (US). McCLANAHAN, Stephen, Francis; 6399 Ironwood Drive, Loveland, OH 45140 (US). ESTES, Paul, Donald; 3096 Struble Road, Cincinnati, OH 45251 (US). GLANDORF, William, Michael; 6933 Keeneland Way, Mason, OH 45040 (US). COX, Edward, Russell; 24 S. Main Street, Germantown, OH 45327 (US).  <b>(74) Agents:</b> REED, T., David et al.; The Procter & Gamble Company, 5299 Spring Grove Avenue, Cincinnati, OH 45217 (US).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> DENTIFRICE COMPOSITIONS CONTAINING POLYPHOSPHATE AND FLUORIDE  <b>(57) Abstract</b>  Disclosed are oral formulations contained in physically separated compartments of a dentifrice dispenser, comprising a first dentifrice composition and a second dentifrice composition. The first dentifrice composition comprises an effective amount of one or more linear polyphosphates having an average chain length of about 4 or more, an effective amount of a buffering agent, and one or more aqueous carriers, wherein the first dentifrice composition has a total water content of from about 5 % to about 20 %. The second dentifrice composition comprises a soluble fluoride ion source, an effective amount of a buffering agent, and one or more aqueous carriers.		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

## DENTIFRICE COMPOSITIONS CONTAINING POLYPHOSPHATE AND FLUORIDE

5

10

### BACKGROUND OF THE INVENTION

Dental calculus, or tartar as it is sometimes called, is a deposit which forms on the surfaces of the teeth at the gingival margin. Supragingival calculus appears principally in the areas near the orifices of the salivary ducts; e.g., on the lingual surfaces of the lower anterior teeth and on the buccal surfaces of the upper first and second molars, and on the distal surfaces of the posterior molars.

Mature calculus consists of an inorganic portion which is largely calcium phosphate arranged in a hydroxyapatite crystal lattice structure similar to bone, enamel, and dentine. An organic portion is also present and consists of desquamated epithelial cells, leukocytes, salivary sediment, food debris, and various types of microorganisms.

As the mature calculus develops, it becomes visibly white or yellowish in color unless stained or discolored by some extraneous agent. This is undesirable from an aesthetic standpoint.

Mechanical removal of calculus periodically by the dentist is routine dental office procedure. A variety of chemical and biological agents have also been suggested to retard calculus formation or to remove calculus after it is formed. Pyrophosphate salts are chemical agents known to have the ability to retard calculus formation as described, for example, in U.S. Patent 4,999,184, to Parran, Jr. et al., issued March 12, 1991, the disclosure of which is incorporated herein by reference in its entirety.

In addition to the pyrophosphate salts, other polyphosphates are also known to help retard calculus formation. U.S. Patent 4,627,977, issued December 9, 1986, to Gaffar et al. discloses the use of linear molecularly dehydrated polyphosphate salt in combination with two additional ingredients which inhibit enzymatic hydrolysis of the polyphosphate. U.S. Patent 4,247,526, to Jarvis et al., issued January 27, 1981, discloses the use of a pharmaceutically acceptable condensed phosphate salt in addition to dicalcium phosphate dihydrate and trimagnesium phosphate. The glassy

polyphosphates are also known to react with ionic fluoride, but only at extreme temperatures (800° C - 900° C). Although polyphosphate containing oral care products are known, there is a continuing need to develop improved products.

5 The present inventors have discovered that certain polyphosphates, in particular, linear polyphosphates with average chain lengths greater than 4 will significantly react with ionic fluoride in oral compositions at ambient temperature and produce monofluorophosphate ions, in addition to altering the pH of the composition. This reaction compromises the ability of the oral composition to provide stable ionic fluoride and polyphosphate to the oral surfaces.

10 Therefore, it is an object of the present invention to provide stable oral formulations comprising two dentifrice compositions which are contained in physically separated compartments, allowing maximum fluoride and polyphosphate delivery to the oral cavity. The first dentifrice composition comprises a polyphosphate and a buffering agent while the second composition comprises a  
15 soluble fluoride ion source and a buffering agent. It is also an object of the present invention to provide a first dentifrice composition comprising a polyphosphate, an alkali metal bicarbonate salt, an alkali metal carbonate salt, calcium peroxide, and an abrasive polishing material and a second composition comprising sodium fluoride, a mixture of pyrophosphate salts, and silica. It is also an object of the  
20 present invention to provide dentifrice formulations with improved antitartar activity through the use of polyphosphates.

These and other objects of the present invention will become readily apparent from the detailed description which follows.

25 All percentages and ratios used herein are by weight of the specific dentifrice composition and not of the overall oral formulation that is delivered, unless otherwise specified. All measurements are made at 25° C, unless otherwise specified.

#### SUMMARY OF THE INVENTION

30 The present invention relates to an oral formulation contained in physically separated compartments of a dentifrice dispenser, comprising a first dentifrice composition comprising an effective amount of one or more linear polyphosphates having an average chain length of about 4 or more, an effective amount of a buffering agent, from about 50% to about 99% of one or more aqueous carriers, wherein the first dentifrice composition has a total water content of from about 5%  
35 to about 20%; and a second dentifrice composition comprising a soluble fluoride source capable of providing from about 50 ppm to about 3500 ppm of free fluoride

ions, an effective amount of a buffering agent, and from about 70% to about 99% of one or more aqueous carriers.

#### DETAILED DESCRIPTION OF THE INVENTION

The oral formulation of the present invention may be in the form of a toothpaste or dentifrice. The term "dentifrice", as used herein, means paste, gel, or liquid formulations unless otherwise specified. The dentifrice composition may be in any desired form, such as deep striped, surface striped, multilayered, having the gel surrounding the paste, or any combination thereof. Each dentifrice composition will be contained in a physically separated compartment of a dispenser and dispensed side-by-side.

The term "dispenser", as used herein, means any pump, tube, or container suitable for dispensing toothpaste.

The term "oral formulation" as used herein means the total dentifrice that is delivered to the oral surfaces. The oral formulation is a combination of the two or more dentifrice compositions. The oral formulation is a product, which in the ordinary course of usage, is not intentionally swallowed for purposes of systemic administration of particular therapeutic agents, but is rather retained in the oral cavity for a time sufficient to contact substantially all of the dental surfaces and/or oral tissues for purposes of oral activity.

The term "aqueous carrier" as used herein means any safe and effective materials for use in the compositions of the present invention. Such materials include abrasive polishing materials, peroxide sources, alkali metal bicarbonate salts, thickening materials, humectants, water, surfactants, titanium dioxide, flavor system, sweetening agents, xylitol, coloring agents, and mixtures thereof.

The present compositions comprise essential components, as well as optional components. The essential and optional components of the compositions of the present invention are described in the following paragraphs.

#### Polyphosphate Source

The present invention includes a polyphosphate source in the first dentifrice composition. A polyphosphate is generally understood to consist of two or more phosphate molecules arranged primarily in a linear configuration, although some cyclic derivatives may be present. Although pyrophosphates are a polyphosphate, the polyphosphates desired are those having around four or more phosphate molecules. The pyrophosphates are discussed separately. The inorganic polyphosphate salts desired include tetrapolyphosphate and hexametaphosphate, among others. Polyphosphates larger than tetrapolyphosphate usually occur as

amorphous glassy materials. Preferred in this invention are the linear "glassy" polyphosphates having the formula:



wherein X is sodium or potassium and n averages from about 6 to about 125.

- 5 Preferred are polyphosphates manufactured by FMC Corporation which are commercially known as Sodaphos ( $n \approx 6$ ), Hexaphos ( $n \approx 13$ ), and Glass H ( $n \approx 21$ ). These polyphosphates may be used alone or in a combination thereof.

The phosphate sources are described in more detail in Kirk & Othmer, *Encyclopedia of Chemical Technology*, Fourth Edition, Volume 18, Wiley-  
10 Interscience Publishers (1996), incorporated herein by reference in its entirety, including all references incorporated into Kirk & Othmer. The polyphosphate source will typically comprise from about 0.5% to about 20%, preferably from about 4% to about 15%, more preferably from about 6% to about 10%, and most preferably from about 7% to about 9%, by weight of the dentifrice composition.

15 Fluoride Ion Source

The second dentifrice composition of the present invention incorporates a soluble fluoride source capable of providing free fluoride ions. Preferred soluble fluoride ion sources include sodium fluoride, stannous fluoride, indium fluoride, and sodium monofluorophosphate. Sodium fluoride is the most preferred soluble  
20 fluoride ion source. Norris et al., U.S. Patent 2,946,725, issued July 26, 1960, and Widder et al., U.S. Patent 3,678,154 issued July 18, 1972, disclose such fluoride ion sources as well as others. Both patents are incorporated herein by reference in their entirety.

The present compositions contain a soluble fluoride ion source capable of  
25 providing from about 50 ppm to about 3500 ppm, and preferably from about 500 ppm to about 3000 ppm of free fluoride ions.

Buffering Agent

The present compositions each contain a buffering agent. Buffering agents, as used herein, refer to agents that can be used to adjust the pH of the compositions  
30 to a range of about pH 6.5 to about pH 10. These agents include alkali metal hydroxides, carbonates, sesquicarbonates, borates, silicates, phosphates, imidazole, and mixtures thereof. Specific buffering agents include monosodium phosphate, trisodium phosphate, sodium hydroxide, potassium hydroxide, alkali metal carbonate salts, sodium carbonate, imidazole, pyrophosphate salts, citric acid, and  
35 sodium citrate. Buffering agents are used at a level of from about 0.1% to about 30%, preferably from about 1% to about 10%, and more preferably from about 1.5% to about 3%, by weight of the present composition.

### Pyrophosphate Salt

Pyrophosphate salts are preferred buffering agents in the second dentifrice composition. The pyrophosphate salts useful in the present compositions include the dialkali metal pyrophosphate salts, tetra alkali metal pyrophosphate salts, and mixtures thereof. Disodium dihydrogen pyrophosphate ( $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$ ), tetrasodium pyrophosphate ( $\text{Na}_4\text{P}_2\text{O}_7$ ), and tetrapotassium pyrophosphate ( $\text{K}_4\text{P}_2\text{O}_7$ ) in their unhydrated as well as hydrated forms are the preferred species. In compositions of the present invention, the pyrophosphate salt may be present in one of three ways: predominately dissolved, predominately undissolved, or a mixture of dissolved and undissolved pyrophosphate.

Compositions comprising predominately dissolved pyrophosphate refer to compositions where at least one pyrophosphate ion source is in an amount sufficient to provide at least about 1.0% free pyrophosphate ions. The amount of free pyrophosphate ions may be from about 1% to about 15%, preferably from about 1.5% to about 10%, and most preferably from about 2% to about 6%, by weight of the composition. Free pyrophosphate ions may be present in a variety of protonated states depending on a the pH of the composition.

Compositions comprising predominately undissolved pyrophosphate refer to compositions containing no more than about 20% of the total pyrophosphate salt dissolved in the composition, preferably less than about 10% of the total pyrophosphate dissolved in the composition. Tetrasodium pyrophosphate salt is the preferred pyrophosphate salt in these compositions. Tetrasodium pyrophosphate may be the anhydrous salt form or the decahydrate form, or any other species stable in solid form in the dentifrice compositions. The salt is in its solid particle form, which may be its crystalline and/or amorphous state, with the particle size of the salt preferably being small enough to be aesthetically acceptable and readily soluble during use. The amount of pyrophosphate salt useful in making these compositions is any tartar control effective amount, and is generally from about 1.5% to about 15%, preferably from about 2% to about 10%, and most preferably from about 2.5% to about 8%, by weight of the composition. Some or all of the tetrasodium pyrophosphate may be undissolved in the product and present as tetrasodium pyrophosphate particles. Pyrophosphate ions in different protonated states (e.g.,  $\text{HP}_2\text{O}_7^{-3}$ ) may also exist depending upon the pH of the composition and if part of the tetrasodium pyrophosphate is dissolved.

Compositions may also comprise a mixture of dissolved and undissolved pyrophosphate salts. Any of the above mentioned pyrophosphate salts may be used.

The pyrophosphate salts are described in more detail in Kirk & Othmer, *Encyclopedia of Chemical Technology*, Third Edition, Volume 17, Wiley-Interscience Publishers (1982), incorporated herein by reference in its entirety, including all references incorporated into Kirk & Othmer.

5 Optional agents to be used in place of or in combination with the pyrophosphate salt include such materials known to be effective in reducing calcium phosphate mineral deposition related to calculus formation. Agents included are synthetic anionic polymers [including polyacrylates and copolymers of maleic anhydride or acid and methyl vinyl ether (e.g., Gantrez), as described, for example,  
10 in U.S. Patent 4,627,977, to Gaffar et al., the disclosure of which is incorporated herein by reference in its entirety; as well as, e.g., polyamino propoane sulfonic acid (AMPS)], zinc citrate trihydrate, diphosphonates (e.g., EHDP; AHP), polypeptides (such as polyaspartic and polyglutamic acids), and mixtures thereof.

#### Aqueous Carriers

15 In preparing the present compositions, it is desirable to add one or more aqueous carriers to the compositions. Such materials are well known in the art and are readily chosen by one skilled in the art based on the physical and aesthetic properties desired for the compositions being prepared. Aqueous carriers typically comprise from about 40% to about 99%, preferably from about 70% to about 98%,  
20 and more preferably from about 90% to about 95%, by weight of the dentifrice composition.

#### Abrasive Polishing Materials

An abrasive polishing material may also be included in the toothpaste compositions. The abrasive polishing material contemplated for use in the  
25 compositions of the present invention can be any material which does not excessively abrade dentin. Typical abrasive polishing materials include silicas including gels and precipitates; aluminas; phosphates including orthophosphates, polymetaphosphates, and pyrophosphates; and mixtures thereof. Specific examples include dicalcium orthophosphate dihydrate, calcium pyrophosphate, tricalcium  
30 phosphate, calcium polymetaphosphate, insoluble sodium polymetaphosphate, hydrated alumina, beta calcium pyrophosphate, calcium carbonate, and resinous abrasive materials such as particulate condensation products of urea and formaldehyde, and others such as disclosed by Cooley et al in U.S. Patent 3,070,510, issued Dec. 25, 1962, incorporated herein by reference. Mixtures of abrasives may  
35 also be used.

Silica dental abrasives of various types are preferred because of their unique benefits of exceptional dental cleaning and polishing performance without unduly



abrading tooth enamel or dentine. The silica abrasive polishing materials herein, as well as other abrasives, generally have an average particle size ranging between about 0.1 to about 30 microns, and preferably from about 5 to about 15 microns. The abrasive can be precipitated silica or silica gels such as the silica xerogels described in Pader et al., U.S. Patent 3,538,230, issued Mar. 2, 1970, and DiGiulio, U.S. Patent 3,862,307, issued Jan. 21, 1975, both incorporated herein by reference. Preferred are the silica xerogels marketed under the trade name "Syloid" by the W.R. Grace & Company, Davison Chemical Division. Also preferred are the precipitated silica materials such as those marketed by the J. M. Huber Corporation under the trade name, "Zeodent", particularly the silica carrying the designation "Zeodent 119". The types of silica dental abrasives useful in the toothpastes of the present invention are described in more detail in Wason, U.S. Patent 4,340,583, issued July 29, 1982, incorporated herein by reference. Silica abrasives described in U.S. patent applications, 08/434,147 and 08/434,149, both filed May 2, 1995, are also herein incorporated by reference. The abrasive in the toothpaste compositions described herein is generally present at a level of from about 6% to about 70% by weight of the composition. Preferably, toothpastes contain from about 10% to about 50% of abrasive, by weight of the dentifrice composition.

#### Peroxide Source

The present invention may include a peroxide source in the first dentifrice composition. The peroxide source is selected from the group consisting of hydrogen peroxide, calcium peroxide, urea peroxide, and mixtures thereof. The preferred peroxide source is calcium peroxide. The following amounts represent the amount of peroxide raw material, although the peroxide source may contain ingredients other than the peroxide raw material. The present composition may contain from about 0.01% to about 10%, preferably from about 0.1% to about 5%, more preferably from about 0.2% to about 3%, and most preferably from about 0.3% to about 0.8% of a peroxide source, by weight of the dentifrice composition.

#### Alkali Metal Bicarbonate Salt

The present invention may also include an alkali metal bicarbonate salt. If present, this bicarbonate salt will be generally be in the first dentifrice composition. Alkali metal bicarbonate salts are soluble in water and unless stabilized, tend to release carbon dioxide in an aqueous system. Sodium bicarbonate, also known as baking soda, is the preferred alkali metal bicarbonate salt. The alkali metal bicarbonate salt also functions as a buffering agent. The present composition may contain from about 0.5% to about 50%, preferably from about 0.5% to about 30%, more preferably from about 2% to about 20%, and most preferably from about 5% to

about 18% of an alkali metal bicarbonate salt, by weight of the dentifrice composition.

Additional Aqueous Carriers

The present invention compositions in the form of toothpastes, typically  
5 contain some thickening material or binders to provide a desirable consistency. Preferred thickening agents are carboxyvinyl polymers, carrageenan, hydroxyethyl cellulose, and water soluble salts of cellulose ethers such as sodium carboxymethylcellulose and sodium hydroxyethyl cellulose. Natural gums such as gum karaya, xanthan gum, gum arabic, and gum tragacanth can also be used.  
10 Colloidal magnesium aluminum silicate or finely divided silica can be used as part of the thickening agent to further improve texture. Thickening agents can be used in an amount from about 0.1% to about 15%, by weight of the dentifrice composition.

Another optional component of the compositions desired herein is a  
15 humectant. The humectant serves to keep toothpaste compositions from hardening upon exposure to air and certain humectants can also impart desirable sweetness of flavor to toothpaste compositions. Suitable humectants for use in the invention include glycerin, sorbitol, polyethylene glycol, propylene glycol, and other edible polyhydric alcohols. The humectant generally comprises from about 0% to 70%,  
20 and preferably from about 15% to 55%, by weight of the composition.

Water employed in the preparation of commercially suitable oral compositions should preferably be of low ion content and free of organic impurities. In the second dentifrice composition, water will generally comprise from about 5% to about 70%, and preferably from about 10% to about 50%, by weight of the  
25 composition herein. The first dentifrice composition will comprise a lower level of water, generally from about 5% to about 20%, preferably from about 7% to about 14%, and more preferably from about 7% to about 12%, by weight of the dentifrice composition. The amounts of water include the free water which is added plus that which is introduced with other materials, such as with sorbitol, silica, surfactant  
30 solutions, and/or color solutions.

The present compositions may also comprise surfactants, also commonly referred to as sudsing agents. Suitable surfactants are those which are reasonably stable and foam throughout a wide pH range. The surfactant may be anionic, nonionic, amphoteric, zwitterionic, cationic, or mixtures thereof. Anionic  
35 surfactants useful herein include the water-soluble salts of alkyl sulfates having from 8 to 20 carbon atoms in the alkyl radical (e.g., sodium alkyl sulfate) and the water-soluble salts of sulfonated monoglycerides of fatty acids having from 8 to 20 carbon

atoms. Sodium lauryl sulfate and sodium coconut monoglyceride sulfonates are examples of anionic surfactants of this type. Other suitable anionic surfactants are sarcosinates, such as sodium lauroyl sarcosinate, taurates, sodium lauryl sulfoacetate, sodium lauroyl isethionate, sodium laureth carboxylate, and sodium dodecyl benzenesulfonate. Mixtures of anionic surfactants can also be employed. Many suitable anionic surfactants are disclosed by Agricola et al., U.S. Patent 3,959,458, issued May 25, 1976, incorporated herein in its entirety by reference. Nonionic surfactants which can be used in the compositions of the present invention can be broadly defined as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkyl-aromatic in nature. Examples of suitable nonionic surfactants include poloxamers (sold under trade name Pluronic), polyoxyethylene, polyoxyethylene sorbitan esters (sold under trade name Tweens), fatty alcohol ethoxylates, polyethylene oxide condensates of alkyl phenols, products derived from the condensation of ethylene oxide with the reaction product of propylene oxide and ethylene diamine, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides, and mixtures of such materials. The amphoteric surfactants useful in the present invention can be broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be a straight chain or branched and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic water-solubilizing group, e.g., carboxylate, sulfonate, sulfate, phosphate, or phosphonate. Other suitable amphoteric surfactants are betaines, specifically cocamidopropyl betaine. Mixtures of amphoteric surfactants can also be employed. Many of these suitable nonionic and amphoteric surfactants are disclosed by Gieske et al., U.S. Patent 4,051,234, issued September 27, 1977, incorporated herein by reference in its entirety. The present composition typically comprises one or more surfactants each at a level of from about 0.25% to about 12%, preferably from about 0.5% to about 8%, and most preferably from about 1% to about 6%, by weight of the composition.

Titanium dioxide may also be added to the present composition. Titanium dioxide is a white powder which adds opacity to the compositions. Titanium dioxide generally comprises from about 0.25% to about 5%, by weight of the composition.

Coloring agents may also be added to the present composition. The coloring agent may be in the form of an aqueous solution, preferably 1% coloring agent in a

solution of water. Color solutions generally comprise from about 0.01% to about 5%, by weight of the composition.

A flavor system can also be added to the compositions. Suitable flavoring components include oil of wintergreen, oil of peppermint, oil of spearmint, clove bud oil, menthol, anethole, methyl salicylate, eucalyptol, cassia, 1-menthyl acetate, sage, eugenol, parsley oil, oxanone, alpha-irisone, marjoram, lemon, orange, propenyl guaethol, cinnamon, vanillin, ethyl vanillin, heliotropine, 4-cis-heptenal, diacetyl, methyl-para-tert-butyl phenyl acetate, and mixtures thereof. Coolants may also be part of the flavor system. Preferred coolants in the present compositions are the paramenthan carboxamide agents such as N-ethyl-p-menthan-3-carboxamide (known commercially as "WS-3") and mixtures thereof. A flavor system is generally used in the compositions at levels of from about 0.001% to about 5%, by weight of the composition.

The present invention may also include xylitol. Xylitol is a sugar alcohol that is used as a sweetener and humectant. Xylitol may provide a therapeutic effect, such as an antibacterial or anticaries effect. The present compositions typically comprise xylitol at a level from about 0.01% to about 25%, preferably from about 3% to about 15%, more preferably from about 5% to about 12%, and most preferably from about 9% to about 11%, by weight of the total composition. Alternatively, if xylitol is used as a sweetener, it may be present at a lower level, such as from about 0.005% to about 5%, by weight of the dentifrice composition.

Sweetening agents can be added to the compositions. These include saccharin, dextrose, sucrose, lactose, maltose, levulose, aspartame, sodium cyclamate, D-tryptophan, dihydrochalcones, acesulfame, and mixtures thereof. Various coloring agents may also be incorporated in the present invention. Sweetening agents and coloring agents are generally used in toothpastes at levels of from about 0.005% to about 5%, by weight of the composition.

The present invention may also include other agents, such as antimicrobial agents. Included among such agents are water insoluble non-cationic antimicrobial agents such as halogenated diphenyl ethers, phenolic compounds including phenol and its homologs, mono and poly-alkyl and aromatic halophenols, resorcinol and its derivatives, bisphenolic compounds and halogenated salicylanilides, benzoic esters, and halogenated carbanilides. The water soluble antimicrobials include quaternary ammonium salts and bis-biquanide salts, among others. Triclosan monophosphate is an additional water soluble antimicrobial agent. The quaternary ammonium agents include those in which one or two of the substitutes on the quaternary nitrogen has a carbon chain length (typically alkyl group) from about 8 to about 20, typically from

about 10 to about 18 carbon atoms while the remaining substitutes (typically alkyl or benzyl group) have a lower number of carbon atoms, such as from about 1 to about 7 carbon atoms, typically methyl or ethyl groups. Dodecyl trimethyl ammonium bromide, tetradecylpyridinium chloride, domiphen bromide, N-tetradecyl-4-ethyl  
5 pyridinium chloride, dodecyl dimethyl (2-phenoxyethyl) ammonium bromide, benzyl dimethylstearyl ammonium chloride, cetyl pyridinium chloride, quaternized 5-amino-1,3-bis(2-ethyl-hexyl)-5-methyl hexa hydropyrimidine, benzalkonium chloride, benzethonium chloride and methyl benzethonium chloride are exemplary of typical quaternary ammonium antibacterial agents. Other compounds are bis[4-  
10 (R-amino)-1-pyridinium] alkanes as disclosed in U.S. Patent 4,206,215, issued June 3, 1980, to Bailey, incorporated herein by reference. Stannous salts such as stannous pyrophosphate and stannous gluconate and other antimicrobials such as copper bisglycinate, copper glysinate, zinc citrate, and zinc lactate may also be included. Also useful are enzymes, including endoglycosidase, papain, dextranase,  
15 mutanase, and mixtures thereof. Such agents are disclosed in U.S. Patent 2,946,725, Jul. 26, 1960, to Norris et al. and in U.S. Patent 4,051,234, September. 27, 1977 to Gieske et al., incorporated herein by reference. Specific antimicrobial agents include chlorhexidine, triclosan, triclosan monophosphate, and flavor oils such as thymol. Triclosan and other agents of this type are disclosed in Parran, Jr. et al.,  
20 U.S. Patent 5,015,466, issued May 14, 1991, and U.S. Patent 4,894,220, Jan. 16, 1990 to Nabi et al., incorporated herein by reference. The water insoluble antimicrobial agents, water soluble agents, and ezymes may be present in either the first or second dentifrice compsoitions. The quaternary ammonium agents, stannous salts, and substituted guanidines are preferably present in the second dentifrice  
25 composition. These agents may be present at levels of from about 0.01% to about 1.5%, by weight of the dentifrice composition.

The first and second dentifrice compositions will be physically separated in a dentifrice dispenser. The dentifrice compositions may be a paste, gel, or any configuration or combination thereof. It is preferred that the first dentifrice  
30 composition be a paste and the second dentifrice composition be a gel. The dispenser may be a tube, pump, or any other container suitable for dispensing toothpaste. Dual compartment packages suitable for this purpose are described in U.S. Patent 4,528,180, issued July 9, 1985; U.S. Patent 4,687,663, issued August 18, 1987; and 4,849,213, issued July 18, 1989, all to Shaeffer, all incorporated herein in  
35 their entirety. The dispenser will deliver approximately equal amounts of each dentifrice composition through an opening. The compositions may intermix once dispensed. Alternatively, the oral formulation may be delivered from a kit

containing two separate dispensers which are used to deliver two dentifrice compositions that are both used simultaneously.

#### Method of Treatment

The present invention compositions additionally relate to a method for  
 5 reducing the incidence of calculus on dental enamel. The method of treatment herein comprises contacting the dental enamel surfaces in the mouth with the oral compositions according to the present invention.

#### Examples & Method of Manufacturing

The following examples further describe and demonstrate embodiments  
 10 within the scope of the present invention. These examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention as many variations thereof are possible without departing from the spirit and scope.

#### EXAMPLE I

15	<u>First Dentifrice Composition</u>		<u>Second Dentifrice Composition</u>	
	<u>Ingredient</u>	<u>Wt. %</u>	<u>Ingredient</u>	<u>Wt. %</u>
	Carboxymethylcellulose	0.60	Color	0.30
20	Water	7.00	Water	33.0
	Flavor	1.00	Flavor	0.40
	Glycerin	43.2	Glycerin	44.514
	Poloxamer 407	5.00	Poloxamer 407	21.00
	Propylene Glycol	5.00	Sodium Fluoride	0.486
25	Sodium Alkyl Sulphate(a)	4.00	Sodium Saccharin	0.30
	Silica	20.0		
	Sodium Carbonate	2.00		
	Sodium Saccharin	0.50		
	Titanium Dioxide	0.50		
30	Xanthan Gum	0.20		
	Glass H Polyphosphate	7.00		
	Polyethylene Glycol	3.00		
	Calcium Peroxide	1.00		

35 (a) 27.9% solution

EXAMPLE II

<u>First Dentifrice Composition</u>		<u>Second Dentifrice Composition</u>	
<u>Ingredient</u>	<u>Wt. %</u>	<u>Ingredient</u>	<u>Wt. %</u>
5 Carboxymethylcellulose	0.60	Carbomer	0.200
Water	7.00	Color	0.400
Flavor	1.00	Water	25.1
Glycerin	26.8	Flavor	0.90
10 Poloxamer 407	5.00	Glycerin	9.00
Propylene Glycol	5.00	Polyethylene Glycol	3.00
Sodium Alkyl Sulphate <sup>(a)</sup>	4.00	Sodium Alkyl Sulphate <sup>(a)</sup>	4.00
Silica	22.0	Silica	22.5
Sodium Bicarbonate	15.0	Sodium Saccharin	0.50
15 Sodium Carbonate	2.00	Sorbitol	29.594
Sodium Saccharin	0.50	Sodium Acid	0.50
Titanium Dioxide	0.50	Pyrophosphate	
Xanthan Gum	0.20	Tetrasodium	3.22
Glass H Polyphosphate	7.00	Pyrophosphate	
20 Polyethylene Glycol	3.00	Xanthan Gum	0.60
Calcium Peroxide	0.40	Sodium Fluoride	0.486

-----  
 (a) 27.9% solution

EXAMPLE III

<u>First Dentifrice Composition</u>		<u>Second Dentifrice Composition</u>	
<u>Ingredient</u>	<u>Wt. %</u>	<u>Ingredient</u>	<u>Wt. %</u>
30 Carboxymethylcellulose	0.60	Carbomer	0.200
Water	7.00	Color	0.400
Flavor	1.00	Water	25.1
Glycerin	24.2	Flavor	0.90
Poloxamer 407	5.00	Glycerin	9.00
35 Propylene Glycol	5.00	Polyethylene Glycol	3.00
Sodium Alkyl Sulphate <sup>(a)</sup>	4.00	Sodium Alkyl Sulphate <sup>(a)</sup>	4.00
Silica	22.0	Silica	22.5
Sodium Bicarbonate	15.0	Sodium Saccharin	0.50
Sodium Carbonate	2.00	Sorbitol	29.644

	Sodium Saccharin	0.50	Sodium Acid	0.75
	Titanium Dioxide	0.50	Pyrophosphate	
	Xanthan Gum	0.20	Tetrasodium	2.92
	Sodaphos Polyphosphate	7.00	Pyrophosphate	
5	Polyethylene Glycol	3.00	Xanthan Gum	0.60
	Calcium Peroxide	3.00	Sodium Fluoride	0.486

-----  
(a) 27.9% solution

10

EXAMPLE IV

<u>First Dentifrice Composition</u>			<u>Second Dentifrice Composition</u>		
	<u>Ingredient</u>	<u>Wt. %</u>		<u>Ingredient</u>	<u>Wt. %</u>
15	Carboxymethylcellulose	0.60		Carbomer	0.200
	Water	7.00		Color	0.400
	Flavor	1.00		Water	22.834
	Glycerin	27.2		Flavor	0.90
	Poloxamer 407	5.00		Glycerin	9.00
20	Propylene Glycol	5.00		Polyethylene Glycol	3.00
	Sodium Alkyl Sulphate <sup>(a)</sup>	4.00		Sodium Alkyl Sulphate <sup>(a)</sup>	4.00
	Silica	22.0		Silica	22.5
	Sodium Bicarbonate	15.0		Sodium Saccharin	0.50
	Sodium Carbonate	2.00		Sorbitol	24.00
25	Sodium Saccharin	0.50		Sodium Acid	2.10
	Titanium Dioxide	0.50		Pyrophosphate	
	Xanthan Gum	0.20		Tetrasodium	2.05
	Glass H Polyphosphate	7.00		Pyrophosphate	
	Polyethylene Glycol	3.00		Xanthan Gum	0.60
30				Sodium Fluoride	0.486
				Triclosan	0.60
				Tetrapotassium	6.830
				Pyrophosphate <sup>(b)</sup>	

-----  
35 (a) 27.9% solution

(b) 60% solution



EXAMPLE V

<u>First Dentifrice Composition</u>		<u>Second Dentifrice Composition</u>	
<u>Ingredient</u>	<u>Wt. %</u>	<u>Ingredient</u>	<u>Wt. %</u>
Carboxymethylcellulose	0.60	Carbomer	0.200
Water	7.00	Color	0.400
Flavor	1.00	Water	25.1
Glycerin	31.2	Flavor	0.90
Poloxamer 407	5.00	Glycerin	9.00
Propylene Glycol	5.00	Polyethylene Glycol	3.00
Sodium Alkyl Sulphate <sup>(a)</sup>	4.00	Sodium Alkyl Sulphate <sup>(a)</sup>	4.00
Silica	27.0	Silica	22.5
Sodium Bicarbonate	5.0	Sodium Saccharin	0.50
Sodium Carbonate	2.00	Sorbitol	33.314
Sodium Saccharin	0.50	Xanthan Gum	0.60
Titanium Dioxide	0.50	Sodium Fluoride	0.486
Xanthan Gum	0.20		
Glass H Polyphosphate	7.00		
Polyethylene Glycol	3.00		
Calcium Peroxide	1.00		

-----  
 (a) 27.9% solution

The first dentifrice compositions are prepared as follows. Add the water and saccharin to a mixing vessel. Disperse the thickening agents, carboxymethyl cellulose and xanthan gum, in the glycerin. Add this mixture of dispersed thickening agents in glycerin to the mixing vessel, mix well, and heat to at least 40° C. Mix the flavor in the Poloxamer and add to the mixture. Add the polyethylene glycol, propylene glycol, and sodium carbonate. Mix well. Next, add the titanium dioxide and the silica. After mixing, add the sodium bicarbonate (if used) and sodium alkyl sulfate. Finally, add the polyphosphate and calcium peroxide (if used). Continue stirring the mixture until homogeneous.

The second dentifrice compositions are prepared by using standard dentifrice making procedures.

## WHAT IS CLAIMED IS:

1. An oral formulation contained in physically separated compartments of a dentifrice dispenser, comprising:
  - a. a first dentifrice composition comprising:
    - (i) an effective amount of one or more linear polyphosphates having an average chain length of 4 or more;
    - (ii) an effective amount of a buffering agent;
    - (iii) from 50% to 99% of one or more aqueous carriers;wherein said first dentifrice composition has a total water content of from 5% to 20%; and
  - b. a second dentifrice composition comprising:
    - (i) a soluble fluoride source capable of providing from 50 ppm to 3500 ppm of free fluoride ions;
    - (ii) an effective amount of a buffering agent; and
    - (iii) from 70% to 99% of one or more aqueous carriers.
2. The oral formulation according to Claim 1 wherein the soluble fluoride source of the second dentifrice composition is sodium fluoride.
3. The oral formulation according to Claim 1 or 2 wherein the one or more polyphosphates of the first dentifrice composition have a chain length of 6 or more and is in an amount of from 0.5% to 20%.
4. The oral formulation according to any of the preceding claims wherein the buffering agent of the second dentifrice composition is a pyrophosphate salt.
5. The oral formulation according to any of the preceding claims wherein the buffering agent in the first and second dentifrice compositions is in an amount of from 0.1% to 30%.
6. The oral formulation according to any of the preceding claims wherein the first dentifrice composition further comprises from 0.01% to 10% of a peroxide source.
7. The oral formulation according to any of the preceding claims wherein the total water content of the first dentifrice composition is from 7% to 14%.

8. An oral formulation contained in physically separated compartments of a dentifrice dispenser, comprising:
- a. a first dentifrice composition comprising:
- (i) from 3% to 10% of one or more linear polyphosphates having an average chain length of 6 or more;
  - (ii) from 0.5% to 40% of an alkali metal bicarbonate salt;
  - (iii) from 0.1% to 30% of an alkali metal carbonate salt;
  - (iv) from 0.01% to 5% of calcium peroxide;
  - (v) from 10% to 70% of an abrasive polishing material; and
  - (vi) from 40% to 87% of one or more aqueous carriers;
- wherein the first dentifrice composition has a total water content of from 7% to 14%; and
- b. a second dentifrice composition comprising:
- (i) an amount of sodium fluoride source capable of providing from 50 ppm to 3500 ppm of free fluoride ions;
  - (ii) from 1.5% to 10% of a pyrophosphate salt;
  - (iii) from 10% to 50% of silica; and
  - (iv) from 40% to 89% of one or more aqueous carriers.
9. The oral formulation according to any of the preceding claims wherein each of the one or more polyphosphates of the first dentifrice composition is selected from the group consisting of linear "glassy" polyphosphates having the formula
- $$\text{XO}(\text{XPO}_3)_n\text{X}$$
- wherein X is sodium or potassium and n averages from about 6 to about 21.
10. The oral formulation according to any of the preceding claims wherein the first dentifrice composition is a paste and the second dentifrice composition is a gel.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/21029

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 A61K7/16 A61K7/18

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 23 13 914 A (BLENDX-WERKE R. SCHNEIDER & CO.) 25 October 1973 ----	1
A	DE 44 46 050 A (LINGNER & FISCHER GMBH) 27 June 1996 -----	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

5 March 1998

Date of mailing of the international search report

18/03/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Glikman, J-F

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/21029

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 2313914 A	25-10-73	GB 1408922 A AT 328089 B DE 2302330 A FR 2170018 A US 4397837 A	08-10-75 10-03-76 16-08-73 14-09-73 09-08-83
DE 4446050 A	27-06-96	WO 9619189 A EP 0794761 A	27-06-96 17-09-97